

Structure of RGL3 and alignment of RasGEFN, RasGEF and RA motifs.

FIG. 1A
RGL3 (710 a.a.)

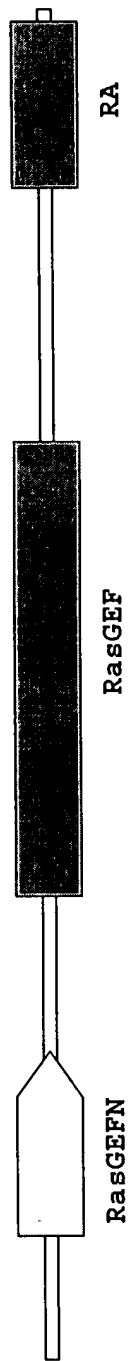


FIG. 1B

RasGEFN motif

	10	20	30	40	50	60
consensus*.....*.....*.....*.....					
RGL3	1 CKGGLIKGGTLEKLIHLEARDK-VDPFTFVETFLTYRSFITTQELLQKLLYRYNAIPP	59				
gi 1354501	64 SKVRVLRARLERLVGELVFGDRE-QDPSFMPAFLATYRTFVPTACLLGFLLP--PMPPP	120				
gi 158471	87 RSSRRLRAGTLEALVRHLLDARTagADMFTPALATHRAFTSTPALFGLVADRLEALES	146				
gi 544403	636 AGVPMIKGATLCKLIERLTYHIY--ADPTFVRTFLTTYRYFCSPQQLLQLLVERFNIPDP	693				
	111 CKVRTVKAGTLEKLVHLEHLPAPQg-SDLSYVTVFLCTYRAFTTQQQVLDLLFKRYGCILP	169				
consensus*.....*.....*.....*.....*.....					
RGL3	60 EGVE-----D-----D-----IWKKEKVNPRRIQ---NRVLNLRLLWV	88				
gi 1354501	121 PPPG-----V-----EIKKTAVQDLSFNknLRVAVSVLGSWL	152				
gi 158471	147 Y-----PPGELERTT---GVAISVLSTWL	167				
gi 544403	694 SLVYqdtgtagaggmgvggDkehknshredwkyRYKEYVQP--VQ---FRVLNVLRHVV	748				
	170 Yss-----eDg-----GPQDQLK---NAISSILGTWL	193				
consensus*.....*.....*.....*.....*.....					
RGL3	89 ENYWQDFEEDPKLNLFLEE-FLELVDDK-KYPGLETSLQNILRRLS	132				
gi 1354501	153 QDHPQDFRDHPahsdllgsvrtflgwaapgsaaekalledflee	198				
gi 158471	168 ASHPEDFGSEVKGQLDRLE-SFLLRRTGYaAREGVVGGSadLIRNLR	212				
gi 544403	749 DHHFYDFEKDPMILLEKLLN-FLEHVNGK-SMRKKWVDSVLKIVQRKN	792				
	194 DQYSEDFCQP-PDFPCLKQlVAYVQLNM-PCSDLERRAHLILAQLE	237				

FIG. 1C
RasGEF motif

	10	20	30	40	50	60	
consensus	1	LLLLDPKELAEQLTLIDFELFRKIDPSELLGSVWGKRSKKS--PSPL--NLERFIERFNE	56				
RGL3	243	LLDFSVEVAEQLTLIDLELFSKVRLYECLGSVWSQRDRPGaaGASP--TVRATVAQFNT	300				
1BKD_S	171	LLTLHPIEIARQLTLLESDLYRAVQPSSELVGSVWTKEDKEI--NSP---NLLKMIRHTTN	225				
gi 544403	363	LLFPDDLVAEQFTLMDAELFKKVVVPYHCLGSIWSQRAKKG--KEHlapTIRATVAQFNN	420				
gi 6919956	239	VLVFLADHLAEQLTLIDAEFLFINLIPSQCLGGLWGHDRDPG--HSHlcpSVRAITVTQFNK	296				
	70	80	90	100	110	120	
consensus	57	VSNWVATEILKQTT-----P--KDRAEllSKFIQVAKHCRELNNFNLSLMAI	100				
RGL3	301	VTGCVLGSVLGAPG-----LaaPQRAQRLEKWIRIAQRCRELNRNFFSSLRAI	346				
1BKD_S	226	LTLWFEKCIIVETEN-----L--EERVAVVSRIIEILQVFOELNNFNGVLEV	269				
gi 544403	421	VANCVITTCIGDQSm-----ka--SDRARVVEHWIEVARECRVLKNFSSLYAI	466				
gi 6919956	297	VAGAVVSSVLGATStgegpgevtirpLRP--PQARLLEKWIRVAEECRLLRNFFSSVYAV	354				
	130	140	150	160	170	180	
consensus	101	VSALSSSPI SRLKKTWEKLP SKYKKLFEELEELLDP SRNFKNYREALSSCN-----	151				
RGL3	347	LSALQSNPIYRLKRSWGA VSREPLSTFRKLSQIFSDENHLSSREILFQEEategsqeed	406				
1BKD_S	270	VSAMNSSPVYRLDHTFEQIPSRQKKILEEAHELSE--DHYKKYLAKLRSIN-----	318				
gi 544403	467	LSALQSNAIHRLKKTWEEVSRGSFRVFQKLSEIFSDeNNYSLSRELLIKEGtskfatlem	526				
gi 6919956	355	VSALQSSPIHRLRAAWGEATRDLSRVFSSLCQIFseeDNYSQSRELLVQEVklqspleph	414				
	190	200	210	220	230	240	
consensus	152	-----LPPCIPFLGVLLKDLTFIDEGNPDFLKN---GLVNF EKRRKIAKIL	194				
RGL3	407	n-----tpgslpskppPGVPVYLGTFITDLVMDTALPDMLEG--DLINFEKRRKEWEIL	459				
1BKD_S	319	-----PPCVPFPGIYLTNlLKTEEGNPEVLKRhgkELINFSKRRKVAEIT	363				
gi 544403	527	nprtrqrqketgviQGTVPYLGTFITDLVMDTAMKDLYG--RLINFEKRRKEFEVI	583				
gi 6919956	415	s-----kkaprsgrsgGVVPYLGTFITDLVMDLDAASKDELEN---GYINFDKRRKEFAVL	467				

FIG. 1C **RasGEF motif**

(Continued)

```

consensus 195 REIRQLQS--QPNLRPNRSDIQSLLOQS--LDSLPEEN---ELYELSLRIEPRV 242
RGL3      460 ARIQQLQRrcQSYTLSPHPPIAAL--HA--QNQLTEEQ----SYRLSRVIEPPa 506
1BKD_S    364 GEIQQYQN--QPYCLRVE-SDIKRFENlnpMGNSMEKEftdYLFNKSLEIEPRN 415
gi 544403 584 AQIKLLQsacNNYSIVPE-EHFGAWFRAM---GRLSEA---ESYNLSCELEPPS 630
gi 6919956 468 SELRRQLQNeRGYNLQPD-HDIQRWLQG---LRPLTEA---QSHRVSCVEVEPPG 514

```

FIG. 1D **RA motif**

```

consensus 1  DQGVLRVYFQDLKPGVAYKTIRVSSSEDTPDVVQLALEKFRLDDEDP EEYALVEVLSGDK 60
RGL3      613 earVIRVSiDNDH-GNLYRSiLLTSQDKAPSVVRRALQKHNVQPQWACDYQLFQVLPGDR 671
1EF5_A    17  DTCiIRiSVEdn-NGNMYKSiMLTSQDKTPAViQRAMSKHNLESDPAEEYELVQViSEDK 75
1RLF      4  DCRIIRVQMELgeDGSVYKSiLVTSQDKAPSViSRVLKKNNRDSAVASEFELVQLLPGDR 63
1LXD_A    15  DCCiIRVSLDVd-NGNMYKSiLVTSQDKAPTViRKAMDKHNLDDEPEDEYELLQIiSEdH 73

consensus 61  ERKLpDDENPLQLRLNLP RDGLSLRFLlKRRD 92
RGL3      672 VLLiPDNANVFYAM----SPVAPRDfMLRRKE 699
1EF5_A    76  ELViPDSANVFYAMNSQVN----FDfILRKKN 103
1RLF      64  ELTiPHSANVFYAMDGAS-----HDFLLRQRR 90
1LXD_A    74  KLKiPENANVFYAMNSAAN----YDFILKKR- 100

```

Structure of the RGL3 gene (Chr. 19p13.2)

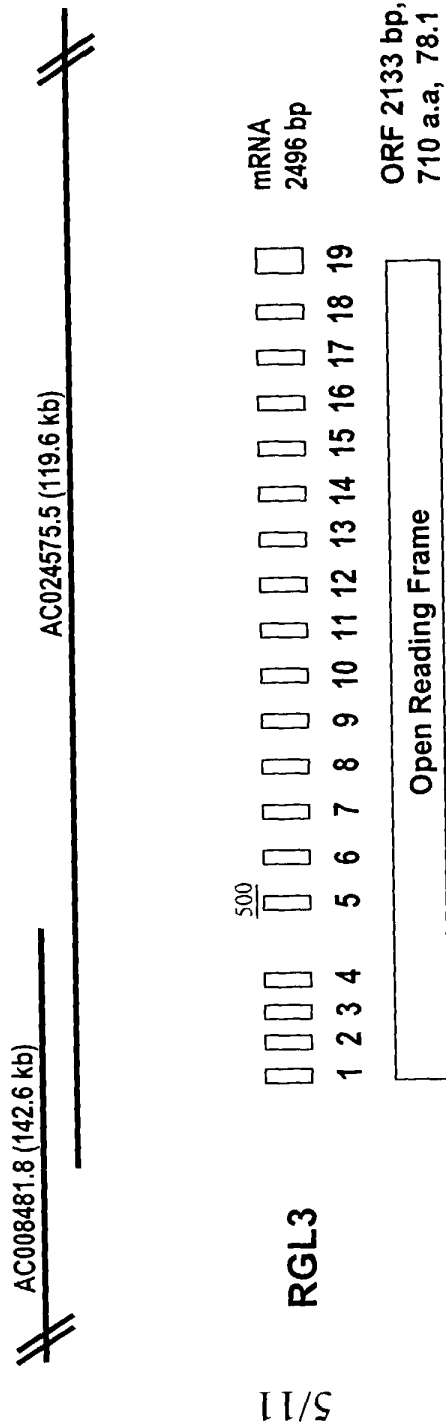


FIG. 2

10060930 .01.2002

6/11

RGL3**nt: SEQ ID NO: 1****aa: SEQ ID NO: 3**

							M	E	R	T	A	G	K	7
CACTGAGAGGGACGGGCGCCAGCC	ATG	GAG	CGC	ACA	GCA	GGC	AAA							45
	E	L	A	L	A	P	L	Q	D	W	G	E	E	20
GAG	CTG	GCC	CTG	GCA	CCG	CTG	CAG	GAC	TGG	GGT	GAA	GAG		84
	T	E	D	G	A	V	Y	S	V	S	L	R	R	33
ACC	GAG	GAC	GGC	GCG	GTG	TAC	AGT	GTC	TCC	CTG	CGG	CGG		123
	Q	R	S	Q	R	R	S	P	A	E	G	P	G	46
CAG	CGC	AGT	CAG	CGC	AGG	AGC	CCG	GCG	GAG	GGC	CCC	GGG		162
	G	S	Q	A	P	S	P	I	A	N	T	F	L	59
GGC	AGC	CAG	GCT	CCC	AGC	CCC	ATT	GCC	AAT	ACC	TTC	CTC		201
	H	Y	R	T	S	K	V	R	V	L	R	A	A	72
CAC	TAT	CGA	ACC	AGC	AAG	GTG	AGG	GTG	CTG	AGG	GCA	GCG		240
	R	L	E	R	L	V	G	E	L	V	F	G	D	85
CGC	CTG	GAG	CGG	CTG	GTG	GGA	GAG	TTG	GTG	TTT	GGA	GAC		279
	R	E	Q	D	P	S	F	M	P	A	F	L	A	98
CGT	GAG	CAG	GAC	CCC	AGC	TTC	ATG	CCC	GCC	TTC	CTG	GCC		318
	T	Y	R	T	F	V	P	T	A	C	L	L	G	111
ACC	TAC	CGG	ACC	TTT	GTA	CCC	ACT	GCC	TGC	CTG	CTG	GGC		357
	F	L	L	P	P	M	P	P	P	P	P	P	G	124
TTT	CTG	CTG	CCA	CCA	ATG	CCA	CCG	CCC	CCA	CCT	CCC	GGG		396
	V	E	I	K	K	T	A	V	Q	D	L	S	F	137
GTA	GAG	ATC	AAG	AAG	ACA	GCG	GTA	CAA	GAT	CTG	AGC	TTC		435

FIG. 3

7/11

N	K	N	L	R	A	V	V	S	V	L	G	S	150
AAC	AAG	AAC	CTG	AGG	GCT	GTG	GTG	TCA	GTG	CTG	GGC	TCC	474
W	L	Q	D	H	P	Q	D	F	R	D	H	P	163
TGG	CTG	CAG	GAC	CAC	CCT	CAG	GAT	TTC	CGA	GAC	CAC	CCT	513
A	H	S	D	L	G	S	V	R	T	F	L	G	176
GCC	CAT	TCG	GAC	CTG	GGC	AGT	GTC	CGA	ACC	TTT	CTG	GGC	552
W	A	A	P	G	S	A	E	A	Q	K	A	E	189
TGG	GCG	GCC	CCA	GGG	AGT	GCT	GAG	GCT	CAA	AAA	GCA	GAG	591
K	L	L	E	D	F	L	E	E	A	E	R	E	202
AAG	CTT	CTG	GAA	GAT	TTT	TTG	GAG	GAG	GCT	GAG	CGA	GAG	630
Q	E	E	E	P	P	Q	V	W	T	G	P	P	215
CAG	GAA	GAG	GAG	CCG	CCT	CAG	GTG	TGG	ACA	GGA	CCT	CCC	669
R	V	A	Q	T	S	D	P	D	S	S	E	A	228
AGA	GTT	GCC	CAA	ACT	TCT	GAC	CCA	GAC	TCT	TCA	GAG	GCC	708
C	A	E	E	E	E	G	L	M	P	Q	G	P	241
TGC	GCG	GAG	GAA	GAG	GAA	GGG	CTC	ATG	CCT	CAA	GGT	CCC	747
Q	L	L	D	F	S	V	D	E	V	A	E	Q	254
CAG	CTC	CTG	GAC	TTC	AGC	GTG	GAC	GAG	GTG	GCC	GAG	CAG	786
L	T	L	I	D	L	E	L	F	S	K	V	R	267
CTG	ACC	CTC	ATA	GAC	TTG	GAG	CTC	TTC	TCC	AAG	GTG	AGG	825
L	Y	E	C	L	G	S	V	W	S	Q	R	D	280
CTC	TAC	GAG	TGC	TTG	GGC	TCC	GTG	TGG	TCG	CAG	AGG	GAC	864
R	P	G	A	A	G	A	S	P	T	V	R	A	293
CGG	CCG	GGG	GCT	GCA	GGC	GCC	TCC	CCC	ACT	GTG	CGC	GCC	903
T	V	A	Q	F	N	T	V	T	G	C	V	L	306
ACC	GTG	GCC	CAG	TTC	AAC	ACC	GTG	ACC	GGC	TGT	GTG	CTG	942
G	S	V	L	G	A	P	G	L	A	A	P	Q	319
GGT	TCC	GTG	CTC	GGA	GCA	CCG	GGC	TTG	GCC	GCC	CCG	CAG	981
R	A	Q	R	L	E	K	W	I	R	I	A	Q	332
AGG	GCG	CAG	CGG	CTG	GAG	AAG	TGG	ATC	CGC	ATC	GCC	CAG	1020

FIG. 3

8/11

R	C	R	E	L	R	N	F	S	S	L	R	A	345
CGC	TGC	CGA	GAA	CTG	CGG	AAC	TTC	TCC	TCC	TTG	CGC	GCC	1059
I	L	S	A	L	Q	S	N	P	I	Y	R	L	358
ATC	CTG	TCC	GCC	CTG	CAA	TCT	AAC	CCC	ATC	TAC	CGG	CTC	1098
K	R	S	W	G	A	V	S	R	E	P	L	S	371
AAG	CGC	AGC	TGG	GGG	GCA	GTG	AGC	CGG	GAA	CCG	CTA	TCT	1137
T	F	R	K	L	S	Q	I	F	S	D	E	N	384
ACT	TTC	AGG	AAA	CTT	TCG	CAG	ATT	TTC	TCC	GAT	GAG	AAC	1176
N	H	L	S	S	R	E	I	L	F	Q	E	E	397
AAC	CAC	CTC	AGC	AGC	AGA	GAG	ATT	CTT	TTC	CAG	GAG	GAG	1215
A	T	E	G	S	Q	E	E	D	N	T	P	G	410
GCC	ACT	GAG	GGA	TCC	CAA	GAA	GAG	GAC	AAC	ACC	CCA	GGC	1254
S	L	P	S	K	P	P	P	G	P	V	P	Y	423
AGC	CTG	CCC	TCA	AAA	CCA	CCC	CCA	GGC	CCT	GTC	CCC	TAC	1293
L	G	T	F	L	T	D	L	V	M	L	D	T	436
CTT	GGC	ACC	TTC	CTT	ACG	GAC	CTG	GTT	ATG	CTG	GAC	ACA	1332
A	L	P	D	M	L	E	G	D	L	I	N	F	449
GCC	CTG	CCG	GAT	ATG	TTG	GAG	GGG	GAT	CTC	ATT	AAC	TTT	1371
E	K	R	R	K	E	W	E	I	L	A	R	I	462
GAG	AAG	AGG	AGG	AAG	GAG	TGG	GAG	ATC	CTG	GCC	CGC	ATC	1410
Q	Q	L	Q	R	R	C	Q	S	Y	T	L	S	475
CAG	CAG	CTG	CAG	AGG	CGC	TGT	CAG	AGC	TAC	ACC	CTG	AGC	1449
P	H	P	P	I	L	A	A	L	H	A	Q	N	488
CCC	CAC	CCG	CCC	ATC	CTG	GCT	GCC	CTG	CAT	GCC	CAG	AAC	1488
Q	L	T	E	E	Q	S	Y	R	L	S	R	V	501
CAG	CTC	ACC	GAG	GAG	CAG	AGC	TAC	CGG	CTC	TCC	CGG	GTC	1527
I	E	P	P	A	A	S	C	P	S	S	P	R	514
ATT	GAG	CCA	CCA	GCT	GCC	TCC	TGC	CCC	AGC	TCC	CCA	CGC	1566

FIG. 3

9/11

I	R	R	R	I	S	L	T	K	R	L	S	A	527
ATC	CGA	CGG	CGG	ATC	AGC	CTC	ACC	AAG	CGT	CTC	AGT	GCG	1605
K	L	A	R	E	K	S	S	S	P	S	G	S	540
AAG	CTT	GCC	CGA	GAG	AAA	AGC	TCA	TCA	CCT	AGT	GGG	AGT	1644
P	G	D	P	S	S	P	T	S	S	V	S	P	553
CCC	GGG	GAC	CCC	TCA	TCC	CCC	ACC	TCC	AGT	GTG	TCC	CCA	1683
G	S	P	P	S	S	P	R	S	R	D	A	P	566
GGG	TCA	CCC	CCC	TCA	AGT	CCT	AGA	AGC	AGA	GAT	GCT	CCT	1722
A	G	S	P	P	A	S	P	G	P	Q	G	P	579
GCT	GGC	AGT	CCC	CCG	GCC	TCT	CCA	GGG	CCC	CAG	GGC	CCC	1761
S	T	K	L	P	L	S	L	D	L	P	S	P	592
AGC	ACC	AAG	CTG	CCC	CTG	AGC	CTG	GAC	CTG	CCC	AGC	CCC	1800
R	P	F	A	L	P	L	G	S	P	R	I	P	605
CGG	CCC	TTC	GCT	TTG	CCT	CTG	GGC	AGC	CCT	CGA	ATC	CCC	1839
L	P	A	Q	Q	S	S	E	A	R	V	I	R	618
CTC	CCG	GCG	CAG	CAG	AGC	TCG	GAG	GCC	CGT	GTC	ATC	CGC	1878
V	S	I	D	N	D	H	G	N	L	Y	R	S	631
GTC	AGC	ATC	GAC	AAT	GAC	CAC	GGG	AAC	CTG	TAT	CGA	AGC	1917
I	L	L	T	S	Q	D	K	A	P	S	V	V	644
ATC	TTG	CTG	ACC	AGT	CAG	GAC	AAA	GCC	CCC	AGC	GTG	GTC	1956
R	R	A	L	Q	K	H	N	V	P	Q	P	W	657
CGG	CGA	GCC	TTG	CAG	AAG	CAC	AAT	GTG	CCC	CAG	CCC	TGG	1995
A	C	D	Y	Q	L	F	Q	V	L	P	G	D	670
GCC	TGT	GAC	TAT	CAG	CTC	TTT	CAA	GTC	CTT	CCT	GGG	GAC	2034
R	V	L	L	I	P	D	N	A	N	V	F	Y	683
CGG	GTG	CTC	CTG	ATT	CCT	GAC	AAT	GCC	AAC	GTC	TTC	TAT	2073
A	M	S	P	V	A	P	R	D	F	M	L	R	696
GCC	ATG	AGT	CCA	GTC	GCC	CCC	AGA	GAC	TTC	ATG	CTG	CGG	2112
R	K	E	G	T	R	N	T	L	S	V	S	P	709
CGG	AAA	GAG	GGG	ACC	CGG	AAC	ACT	CTG	TCT	GTC	TCC	CCA	2151

FIG. 3

10/11

S	*		711
AGC	TGA	GGCAGCCCTGTCCTCTCCACAAGACACAAGTCCCACAGGCAAG	2200
CTTGCGACTCTTCTCCTGGAAAGCTGCCATCCCCCAGTAGAGGCCACTGTGC			2252
TGTGTATCCCAGGACCACCACCCAAGTGTAGCCCATTGGACCCCATCTCTTT			2304
TTCTGACTCTGTTGGTACTAGATCCATATTCCAAAGACATCAGCCCATGGGT			2356
GGCTGGTGGAGAGCTCAATCCCATAAATGTAGAAAGAGGTGGGGCATGGATA			2408
CGTCAAATCCCTCCCCAGAGAAATCTTATAAATGTTAGAGACGCATCAGAAG			2460
TGACAGATGCGGATGAAAATAGTGACCAGAGTTATG			2496

FIG. 3

Tissue Expression profile of RGL3

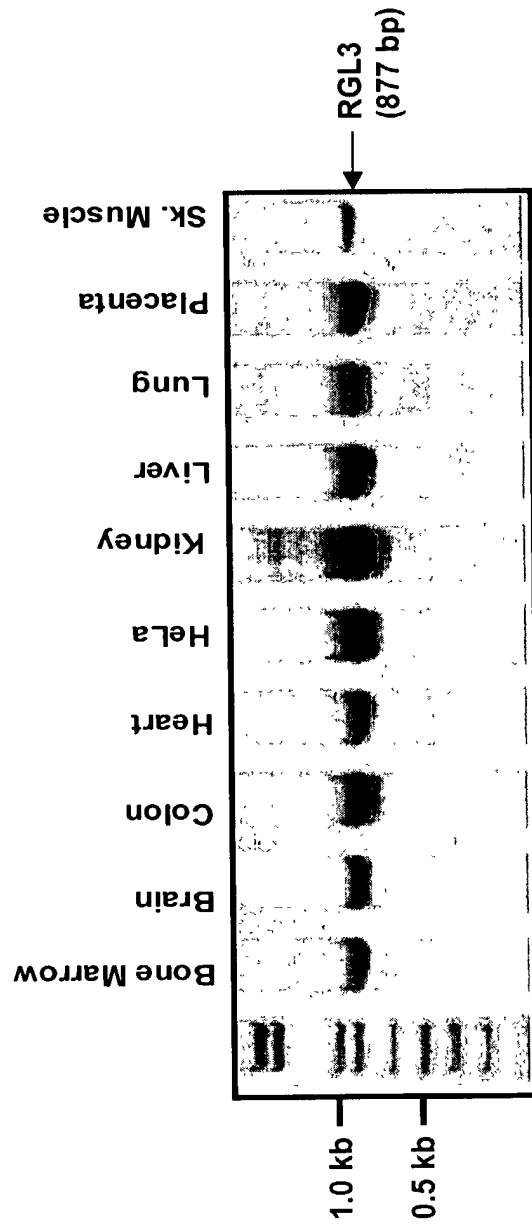


FIG. 4